REMARKS

In the Restriction Requirement that was mailed in this case on October 1, 2002, the Examiner required applicants to elect one of the following two groups of claims:

I. Claims 1-20, drawn to a method of preventing or treating an amyloid-related disease in a subject; and

II. Claims 21-39, drawn to a composition comprising an antigenic amount of an all-D peptide and a pharmaceutical composition comprising such a peptide.

The Examiner also stated that claims 1-39, each in part, were subject to restriction with respect to specific sequences in this application (SEQ ID NOs:1-65).

In reply to the Restriction Requirement, applicants elect for examination in this application the invention of Group I, claims 1-20, and the sequence of SEQ ID NO:15, leaving claims 21-39 to be withdrawn from consideration if the Requirement is maintained. This election is made with traverse, for the reasons discussed below.

First, applicants note that, in an effort to facilitate examination in the event that the Restriction Requirement is maintained, the remaining claims in which sequence identification numbers occur have been amended to specify that the peptides of these claims comprise the sequence of SEQ ID NO:15. Applicants also note that the sequence of SEQ ID NO:15 is present in other sequences in this application as well, including SEQ ID NOs:1-4, 7-9, 12, 17, 20, 23, 25, 27-29, 52, 55, 58, 61, and 64. Thus, if it is

determined that methods employing peptides comprising the sequence of SEQ ID NO:15 are patentable, applicants submit that claims including SEQ ID NOs:1-4, 7-9, 12, 17, 20, 23, 25, 27-29, 52, 55, 58, 61, and 64 should also be considered patentable and be rejoined with this application.

Applicants further note that they respectfully disagree with the Examiner's requirement that they elect only one of SEQ ID NOs:1-65 for examination in this application. One criterion for a proper requirement for restriction is that there must be a serious burden on the examiner in the absence of restriction. M.P.E.P. § 803.04. In the case of applications including nucleotide sequences, it has been deemed that sequences encoding different proteins may be subject to restriction, because the sequences represent structurally distinct chemical compounds and are unrelated to one another. Nonetheless, to aid the biotechnology industry, the Commissioner has partially waived the requirements of 35 U.S.C. § 121 to allow a reasonable number of sequences to be searched in a single application, which is normally ten. M.P.E.P. § 803.04.

Applying the principles set forth above to peptide sequences, it would seem that the present applicants should be allowed to have at least ten peptide sequences examined in this application. Applicants respectfully submit that they should be allowed to have even more than ten sequences examined, because unlike the unrelated nucleic acid sequences discussed above, the sequences of many of the peptides of the present claims are indeed highly related to one another. In particular, many of the peptides of the present

claims are fragments of a peptide, designated Aβ (see, e.g., SEQ ID NO:1) which, though larger than the claimed peptides, is only 39-43 amino acids in length. These peptides include numerous overlapping sequences, and applicants thus submit that it would not be unduly burdensome for the Examiner to search them. For example, SEQ ID NOs:1-4, 7-9, 17, 20, 23, 25, and 27-29 are fragments of Aβ that each include the core sequence KLVF (SEQ ID NO:15). The sequences of these peptides differ from one another only in the number of Aβ amino acids that are present on the amino and/or carboxyl terminal ends of the peptides, and may readily be searched together. Similarly, SEQ ID NOs:1-4, 6, 8, 9, and 29 are fragments of Aβ that each include the core sequence HHQK (SEQ ID NO:32), and these sequences differ from one another only in the amino and/or carboxyl terminal Aβ sequences that they include; again these sequences may be searched together with no undue burden. Moreover, as can be seen by inspection of the complete Aβ sequence (see, e.g., SEQ ID NO:1), the core sequences noted above, KLVF and HHQK overlap with one another (the K at the carboxyl terminus of HHQK is the same amino acid in Aβ as the amino terminal K in KLVF) and, thus, applicants submit that it would not require an undue burden to examine, for example, each of these two groups of highly related sequences. Applicants further submit that other sequences present in this application correspond to peptides that include only single substitutions of naturally occurring Aβ sequences (see, e.g., SEQ ID NOs:11-13, 16, 18, 19, 21, 24, 26, 51, 52, 54, 55, 57, 58, 60, 61, 63, and 64), and thus that there would not be an undue burden in

searching these sequences as well.

Finally, applicants respectfully submit that the requirement to select a sequence for examination in this case should not be applied to all of the claims, as is stated in the Restriction Requirement. Rather, the requirement should only be applied, if at all, to the claims that specifically mention sequences: claims 8, 10, 17, 19, 27, 29, 36, and 38. Thus, applicants submit that all of the other claims, which are generic with respect to sequences, should be examined generically in this regard.

Applicants respectfully request reconsideration of the Requirement for Restriction. Enclosed is a Petition to extend the period for replying to the Restriction Requirement for one month, to and including December 2, 2002 (as December 1, 2002 falls on a Sunday) and a check in payment of the required extension fee. If there are any additional charges or any credits, please apply them to Deposit Account No. 03-2095.

Respectfully submitted,

Date: December 2 2002

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Version of Amendment Showing Changes Made

Page 43, lines 8-10 have been amended as follows.

SEQ ID NO: 27 Lys-Leu-Val-Phe-Phe-Ala-[Gln]Glu (all-D)

SEQ ID NO: 28 Lys-Leu-Val-Phe-Phe-Ala-[Gln]Glu-NH_2 (all-D)

SEQ ID NO: 29 His-His-Gln-Lys-Leu-Val-Phe-Phe-Ala-[Gln]Glu (all-D)

Page 44, lines 15-17 of the specification have been amended as follows.

The following are exemplary compounds derived from compound 20 [18] (all-D KLVFFA-NH_2; SEQ ID NO: 20 [18]) by substituting one or two amino acid residue(s) with other amino acids.

Claims 1-4, 6-8, and 12-17 have been amended as follows.

1. (Amended) A method for preventing or treating an amyloid-related disease in a subject, comprising: administering to the subject an antigenic amount of an all-D peptide, wherein said all-D peptide elicits the production of antibodies against said all-D peptide and induces an immune response by said subject, thereby preventing or reducing amyloid-induced neurodegeneration [cellular toxicity] or amyloid fibril formation.

2. (Amended) A method for preventing or treating an amyloid-related disease in a subject, comprising: administering to the subject an antigenic amount of an all-D peptide, wherein said all-D peptide interacts with an amyloid protein, elicits the production of antibodies against said all-D peptide, and induces an immune response by said subject, thereby preventing or reducing amyloid-induced cellular

toxicity or amyloid fibril formation.

3. (Amended) The method of claim 1, wherein said all-D peptide comprises a peptide of [interacts with] at least one region of an amyloid fibril or an amyloid protein, said region being selected from the group consisting of: Aβ(1-42), C-terminal region, β sheet region, GAG-binding site region, cellular [macrophage] adherence region, immunogenic fragments thereof, protein conjugates thereof, immunogenic derivative peptides thereof, immunogenic peptides thereof, and immunogenic peptidomimetics thereof.

4. (Amended) The method of claim 3, wherein said all-D peptide further comprises:

(a) an N-terminal substituent selected from the group consisting of:

hydrogen;

lower alkyl group consisting of acyclic or cyclic having 1 to 8 carbon atoms;

aromatic group;

heterocyclic group; and

acyl group; and

(b) a C-terminal substituent selected from the group consisting of hydroxy, alkoxy, aryloxy, unsubstituted and substituted amino groups.

6. (Amended) The method of claim 4 [1], wherein said all-D peptide further comprises an acid functional group, or a pharmaceutically acceptable salt or ester form thereof.

7. (Amended) The method of claim 4 [3], wherein said all-D peptide further comprises a base functional group, or a pharmaceutically acceptable salt form thereof.

8. (Amended) The method of claim 3 [4], wherein said all-D peptide comprises SEQ ID NO:15 [is selected from the group consisting of SEQ ID NOS: 1-50].

12. (Amended) A method for preventing or treating an amyloid-related disease in a subject, comprising:

administering to the subject an antigenic amount of a peptide having Formula I:

R'—(P)—R" (I)

wherein

P is an all-D peptide [that interacts with at least one region] of an amyloid fibril or an amyloid protein selected from the group consisting of: Aβ(1-42), C-terminal region, β sheet region, GAG-binding site region, cellular [macrophage] adherence region, immunogenic fragments thereof, protein conjugates thereof, immunogenic derivative peptides thereof, immunogenic peptides thereof, and immunogenic peptidomimetics thereof;

R' is an N-terminal substituent selected from the group consisting of:

hydrogen;

lower alkyl group consisting of acyclic or cyclic having 1 to 8 carbon atoms;

aromatic group;

heterocyclic group; and

acyl group; and

R" is a C-terminal substituent selected from the group consisting of hydroxy group, alkoxy group, aryloxy group, unsubstituted group, and substituted amino group.

13. (Amended) The method of claim 12 [11], wherein said all-D peptide elicits the production of antibodies against said all-D peptide, and induces an immune response by said subject, thereby preventing or reducing amyloid-induced neurodegeneration [cellular toxicity] or amyloid fibril formation.

14. (Amended) The method of claim 12 [11], wherein said alkyl or aromatic group is further substituted with a group selected from the group consisting of halide, hydroxyl, alkoxyl, aryloxyl, hydroxycarbonyl, alkoxylcarbonyl, aryloxycarbonyl, carbamyl, unsubstituted amino, substituted amino, sulfo, alkyloxysulfonyl, phosphono and alkoxyphosphonyl groups.

15. (Amended) The method of claim 12 [11], wherein said all-D peptide further comprises an acid functional group, or a pharmaceutically acceptable salt or ester form thereof.

16. (Amended) The method of claim 12 [11], wherein said all-D peptide further comprises a base functional group, or pharmaceutically acceptable salt form thereof.

17. (Amended) The method of claim 12 [11], wherein said all-D peptide comprises SEQ ID NO:15 [is selected from the group consisting of SEQ ID NOS: 1-50].